Case Report Rapport de cas

The use of alfaxalone and remifentanil total intravenous anesthesia in a dog undergoing a craniectomy for tumor resection

Leon N. Warne, Thierry Beths, Sandra Fogal, Sébastien H. Bauquier

Abstract — A 7-year-old castrated border collie dog was anesthetised for surgical resection of a hippocampal mass. Anesthesia was maintained using a previously unreported TIVA protocol for craniectomy consisting of alfaxalone and remifentanil. Recovery was uneventful, and the patient was discharged from hospital. We describe the anesthetic management of this case.

Résumé — Protocol anesthésique associant alfaxalone et rémifentanil lors d'une résection d'une masse intracrânienne chez un border collie. Ce rapport de cas décrit la prise en charge anesthésique ainsi que le protocole d'anesthésie par perfusion intraveineuse utilisé lors d'une résection chirurgicale d'une masse hippocampale sur un border collie de 7 ans. La combinaison alfaxalone et rémifentanil, en tant qu'agents anesthésiques principaux, fut utilisée et le patient récupéra sans complication.

(Traduit par Sébastien Bauquier)

Can Vet J 2014;55:1083–1088

Anesthesia for neurosurgical patients undergoing intracranial procedures should provide hemodynamic stability, maintain cerebral perfusion pressure (CPP), reduce the cerebral metabolic rate (CMR), preserve cerebral autoregulation, avoid increases in intracranial pressure (ICP), and guarantee rapid recovery (1). Volatile anesthetics (e.g., isoflurane, sevoflurane, desflurane) are dose-dependent cerebral vasodilators that affect cerebral autoregulation and ICP, increasing the risk of cerebral ischemia (2). In contrast, most intravenous anesthetic, analgesic, and sedative drugs maintain a linear correlation between reduction in cerebral blood flow (CBF) and CMR, autoregulation of cerebral perfusion and CO_2 responsiveness, and have minimal effect on ICP (2,3). Balanced TIVA typically consists of an intravenous hypnotic agent (e.g., propofol or alfaxalone) and one or several intravenous analgesics (e.g., fentanyl or remifentanil, lidocaine) excluding simultaneous administration of any inhalant anesthetics (4).

To the authors' knowledge the concurrent use of remifentanil and alfaxalone has not been reported in any species. Alfaxalone (3α-hydroxy-5α-pregnane-11,20-dione) is a synthetic neuroactive steroid, which interacts with the gamma-aminobutyric acid $(GABA)_A$ receptor producing anesthesia and muscle relaxation. This water-insoluble molecule in a co-formulation with alfadolone and solubilized in a polyoxyethylated castor-oil based surfactant (cremophor EL), has previously been used for neurosurgical anesthesia in humans (Althesin; GlaxoSmithKline, Middlesex, UK) (5). Alfaxalone was also used as an anesthetic agent in cats and dogs (Saffan; Schering Plough Animal Health, Union, New Jersey, USA).

Saffan anesthesia became associated with side-effects in several species. In dogs, cremophor EL induces an anaphylactoid hypersensitivity reaction and a subsequent fall in arterial blood pressure with urticaria and erythema (6). The current, cremophor-free formulation of alfaxalone was subsequently developed by solubilizing alfaxalone in 2-hydroxypropyl-β-cyclodextrin. This formulation is registered for use in dogs and cats in Australia, Canada, and Europe, and recently (August 2014) the United States. The effects of this new formulation on cerebral hemodynamics are unknown; however, considering the properties of the older alfaxalone-alfadolone co-formulation, a decrease in CBF would be expected (5,7,8).

Remifentanil is a synthetic full μ-agonist opioid analgesic characterized by a rapid onset of action and ultra-short duration of action due to its clearance by plasma esterases. The pharmacokinetics of remifentanil make it ideal for TIVA because of a lack of cumulative effects (9). Remifentanil is routinely used as part of TIVA protocols in humans and as an intraoperative analgesic in dogs (10,11).

There is limited information regarding neuroanesthesia in veterinary patients. This report presents the anesthetic management and considerations in a dog undergoing surgical resection of an intracranial mass and evaluates the effectiveness of TIVA with alfaxalone and remifentanil as a novel anesthetic protocol for neurosurgery in the dog.

Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Werribee, Victoria, Australia (Warne, Beths, Bauquier); Veterinary Anaesthesia Services International, Zürcherstrasse 39, 8400 Winterthur, Switzerland (Fogal).

Address all correspondence to Dr. Leon N. Warne; e-mail: lwarne@unimelb.edu.au

Case description

After an MRI study, a 20.3 kg 7-year-old castrated male border collie dog with an 8-month history of generalized seizures was diagnosed with a lesion in the right medial temporal lobe. There was evidence of a mass-effect but no clinical signs of increased ICP. The dog was referred for surgical resection of the lesion.

Upon admission for surgery, the patient's demeanor was calm, alert, and responsive. Physical and neurological examination were unremarkable. Hematological and serum biochemical analysis performed 12 h earlier were unremarkable. Current medications on admission included phenobarbital [3.5 mg/kg body weight (BW), PO, q12h], prednisolone (0.75 mg/kg BW, PO, q24h), potassium bromide (20 mg/kg BW, PO, q12h), and gabapentin (10 mg/kg BW, PO, q8h). The last dose of these drugs was administered 3 h prior to anesthesia. Food was withheld 12 h prior to anesthesia. Maropitant (Cerenia; Pfizer, West Ryde, NSW, Australia), 1.0 mg/kg BW, SC was administered 1 h prior to premedication.

Anesthetic management

Methadone (Physeptone Injection; Sigma Pharmaceuticals, Croydon, VIC, Australia), 0.4 mg/kg BW, IM, was administered in the abaxial muscles for sedation, and to facilitate catheter placement, 55 min prior to anesthesia. The right cephalic vein was catheterized with a 20-gauge, over-the-needle IV catheter. Five minutes prior to anesthesia induction the patient was pre-oxygenated via facemask. During this time the patient was connected to a multi-parameter anesthesia monitor (Advisor Vital Signs Monitor V9203; SurgiVet, Smiths Medical PM, Waukesha, Wisconsin, USA), which continuously displayed a lead II ECG, heart rate (HR), plethysmographic oxygen saturation (SpO_2), and non-invasive blood pressure (NIBP). Anesthesia was induced with an IV combination of fentanyl (Fentanyl Injection; Hospira, Mulgrave, Australia), 5 μg/kg BW, lidocaine (Lignocaine 20; Troy Laboratories, Smithfield, NSW, Australia), 2.0 mg/kg BW, followed by alfaxalone (Alfaxan, Jurox, Rutherford, NSW, Australia), which was titrated slowly to effect (total dose 1.5 mg/kg BW). A cuffed 9.0-mm ID endotracheal tube (ETT) was placed and connected to a rebreathing circle system (Small Animal Anesthesia Machine V701001; SurgiVet, Smiths Medical PM). End-tidal partial pressure of carbon dioxide ($PE'CO_2$) was obtained via a calibrated side-stream gas analyser component of the multi-parameter monitor. Intermittent positive-pressure ventilation (IPPV) with 100% oxygen was initiated following intubation using a pressure-cycled mechanical ventilator (ULCO Campbells EV500 Electronic Ventilator; ULCO Medical, Marrickville, NSW, Australia). Peak inspiratory pressure (PIP) was set between 10 and 12 cm H_2O, and respiratory rate (RR) was adjusted to maintain $PE'CO_2$ at 30 ± 2 mmHg.

The patient was positioned in right lateral recumbency with the head supported to keep the thoracic and cervical spine straight. Occlusion of the jugular veins was avoided except for a brief period during placement of a 5.5 Fr, 8-cm triple-lumen jugular catheter into the left jugular vein. The left dorsal pedal artery was catheterized with a 22-gauge, over-the-needle IV catheter. Both the jugular and pedal artery catheters were connected to 2 electronic pressure transducers (DTX Plus DT-4812 Disposable Pressure Transducer Sets; BD Medical Systems, North Ryde, NSW, Australia) positioned at the level of the sternum to measure central venous pressure (CVP) and arterial blood pressure (IBP), respectively. Central venous pressure and IBP were continuously displayed on the multi-parameter monitor. Once instrumented the patient was placed in sternal recumbency for surgical site preparation with the head slightly elevated. A forced warm air blanket was used throughout the procedure to mititgate intraoperative hypothermia (Bair Hugger; Advanced Anaesthesia Specialists, NSW, Australia). Body temperature was measured using an intra-esophageal temperature probe and continuously displayed on the multi-parameter monitor.

Table 1. Variation in heart rate, mean arterial blood pressure, and central venous pressure during the perioperative period

Time	Immediately prior to AI	AI to start of surgery range (min, max)	Anesthesia maintenance (intraoperative) range (min, max)
HR (bpm)	80	60, 100	80, 96
MAP (mmHg)	95	70, 95	85, 100
CVP (mmHg)	N/A	6, 8	5, 7

AI — anesthesia induction; HR — heart rate; bpm — beats/min; MAP — mean arterial blood pressure; CVP — central venous pressure; N/A — variable not measured.

Anesthesia was maintained via TIVA using a triple-channel infusion pump (Baxter Colleague 3CX Volumetric Infusion Pump; Baxter Healthcare, Deerfield, Illinois, USA), consisting of alfaxalone at an initial constant rate infusion (CRI) of 0.15 mg/kg BW/min, IV and, starting 15 min prior to the commencement of surgery, remifentanil (Remifentanil HCL 1 mg; GlaxoSmithKline, Boronia, VIC, Australia) at 0.2 μg/kg BW/min, IV. The rate of remifentanil was increased to 0.3 μg/kg BW/min at the commencement of surgery. The infusion rate of alfaxalone ranged from 0.10 to 0.15 mg/kg BW/min during surgery and was adjusted according to changes in the anesthetic depth of the patient. Criteria used to assess depth of anesthesia included HR; IBP; attempts to breathe against the ventilator, spontaneous movement, anal tone and $PE'CO_2$ changes. Incremental increases or decreases (0.01 mg/kg BW/min) in the alfaxalone infusion rate were made if the depth of anesthesia was deemed to be inadequate or excessive. An IV bolus of alfaxalone (0.5 mg/kg BW) was administered if voluntary movement occurred. Alfaxalone infusion rate was recorded every 5 min, along with all physiological parameters displayed on the multi-parametric display. Sodium chloride (NaCl) was infused intravenously (0.9% Sodium Chloride Intravenous Infusion; Baxter Healthcare Pty, Toongabbie, NSW, Australia), 10 mL/kg BW per hour for the first hour, the rate was then reduced to 5 mL/kg BW per hour for the duration of anesthesia. Cefazolin was administered (Cefazolin; Sandoz Pty, Pyrmont, NSW, Australia), 22 mg/kg BW, IV, 60 min prior to surgical incision and then every 90 min throughout surgery. When required, glycopyrrolate (Glycosate Vet Injection; Nature Vet Pty, Glenorie, NSW, Australia), 0.005 to 0.01 mg/kg BW,

Table 2. Arterial blood gas values, end tidal partial pressure of carbon dioxide, and alveolar dead space ventilation in a border collie dog undergoing general anesthesia for brain tumor resection

Time (min)	pH	$PECO_2$ (mmHg)	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	HCO_3 (mmol/L)	BE (mmol/L)	VDAlv/VT (%)	Glucose (mmol/L)	Lactate (mmol/L)
45	7.363	28	36.4	421[a]	20.0	−4.3	23.1	4.9	4.7
135	7.407	30	35.9	574[a]	22.7	−1.7	16.4	5.1	3.9
225	7.395	28	34.1	560[a]	20.2	−3.7	17.8	5.6	6.3
315	7.328	29	34.5	560[a]	17.6	−7.3	15.9	5.1	7.3
15 min after extubation	7.316	—	39.1	82.9[b]	19.1	−5.8	—	7.0	5.5

$PECO_2$ — end tidal partial pressure of carbon dioxide; $PaCO_2$ — partial pressure of carbon dioxide in arterial blood; PaO_2 — arterial partial pressure of oxygen (at sea level); HCO_3 — bicarbonate; BE — base excess; VDAlv/VT — alveolar dead space ventilation.
[a] Sample taken during ventilation with a fraction of inspired oxygen content ($FI'O_2$) of 100%.
[b] Sample taken during spontaneous ventilation on room air only.

IV was administered to maintain HR above 60 beats/min (bpm) and dopamine (DBL® Sterile Dopamine Concentrate; Hospira Australia Pty, Mulgrave, VIC, Australia), 5 to 10 μg/kg BW per min, IV was administered to effect to maintain a mean arterial blood pressure (MAP) above 80 mmHg. Arterial blood samples were collected anaerobically from the arterial catheter and analyzed immediately for blood-gases (ABG), pH, electrolytes, glucose, and lactate (ABL 800 Basic analyser, Radiometer, Copenhagen, Denmark) at 45, 135, 225, 315 min post-induction of anesthesia and 15 min post-extubation (45 min after the alfaxalone CRI was discontinued). The alveolar dead space ventilation (VDAlv/VT) was calculated using a modified-Bohr equation (12):

$$VDAlv/VT = [(PaCO_2 — PECO_2)/PaCO_2]$$

Surgery consisted of a craniectomy and right-sided temporal lobectomy performed via an extended lateral rostrotentorial. Heart rate, MAP, and CVP variability during the perioperative period are summarized in Table 1. Body temperature ranged from 35.6°C during surgical site preparation to 37.2°C at extubation.

Electrolyte values remained within established reference ranges. Blood-gases, pH, $PE'CO_2$, VDAlv/VT, HCO_3, base excess (BE), glucose, and lactate results are summarized in Table 2. Thirty minutes prior to the completion of surgery a bolus of methadone 0.2 mg/kg BW was administered IV and 5 min later the remifentanil infusion was discontinued.

Recovery

Following skin closure, the patient was transferred to the intensive care unit for recovery. Total anesthesia time (from induction to cessation of alfaxalone delivery) was 7 h and 15 min. The ETT remained in place until attempts were made to breathe spontaneaously, $PE'CO_2$ was maintained between 35 to 45 mmHg and the laryngeal reflexes returned approximately 30 min after the alfaxalone infusion was discontinued. The patient made a quiet, calm recovery, and did not display signs of anxiety or dysphoria. He was deemed to not be exhibiting signs of pain when assessed immediately after extubation, using The Melbourne Pain Scale (score of 0 out of 27) (13). Regular assessment of pain, vital-signs and physiological parameters was conducted every 2 h until discharge with no abnormalities detected. The patient was able to ambulate unassisted 2 d following surgery and was discharged home after 6 d hospitalization, with no seizures or significant postoperative complications. Postoperative analgesia consisted of methadone, 0.2 mg/kg BW, IV, every 4 to 6 h as required, based on evaluation of pain.

Discussion

Prior to the present case the authors had routinely used a TIVA protocol of propofol and remifentanil as the advantages of this regime for neurosurgical procedures are well-documented (14,15). However due to a propofol shortage, alfaxalone-based TIVA was used instead. Although the effects of alfaxalone on cerebral hemodynamics in the dog are unknown, considering the properties of the older alfaxalone-alfadolone co-formulation in dogs, cats, and humans, a decrease in CMR CBF and ICP, would be expected (5,7,8,16–18).

Alfaxalone anesthesia is characterized by a rapid, smooth induction and recovery. Alfaxalone causes a dose-dependent reduction in cardiorespiratory variables following induction of anesthesia similar to propofol (19). In dogs, alfaxalone is rapidly cleared from the plasma and cumulative effects are low. Alfaxalone has a high total body clearance in the dog (55 mL/min/kg), corresponding to 50% to 60% of cardiac output, which favors its application as a TIVA for prolonged procedures (20). Recovery from alfaxalone anesthesia depends more on drug metabolism than redistribution. Alfaxalone undergoes extensive hepatic metabolism with the major metabolites being excreted in the urine leading to a dose-dependent duration of action and relatively rapid recovery from anesthesia (6). Findings from an in-house study by Jurox in 2005, demonstrated that alfaxalone is metabolized *in vitro* by canine hepatocytes through both Phase-I (cytochrome P450 dependent) and Phase-II (glucuronide and sulfate conjugation dependent) enzymatic systems (21). Phase-I alfaxalone metabolites were allopregnatrione; 3β-alfaxalone; 20-hydroxy-3β-alfaxalone; 20-hydroxyalfaxalone; and 2α-hydroxyalfaxalone. Phase-II metabolites were alfaxalone glucuronide; 2α-hydroxyalfaxalone glucuronide; and 20-hydroxyalfaxalone sulphate. The major alfaxalone conjugate was alfaxalone glucuronide. Because glucuronidation plays a major role in the metabolism of alfaxalone, hepatic insufficiency is likely to prolong anesthetic recovery time.

Gabapentin was administered for 7 d prior to surgery as part of a multimodal approach to pain management. Gabapentin has antiallodynic and antihyperalgesic properties useful for treating neuropathic pain (22). In humans preemptive gabapentin has reduced anesthetic and analgesic requirements during and after craniotomy surgery (23). Avoidance of perioperative vomiting

decreases patient discomfort, risk of aspiration pneumonia, and morbidity associated with increased ICP (24). Maropitant was administered prior to premedication. Maropitant is a neurokinin-1 receptor antagonist that has been approved to prevent and treat vomiting in dogs secondary to a broad-spectrum of emetic stimuli (24,25).

Methadone is a pure μ-opioid agonist suitable for the treatment of moderate to severe pain, with pharmacological properties similar to morphine and an antinociceptive efficacy 10 to 50 times greater (26). Unlike morphine, methadone does not induce emesis in the dog (27). Methadone also acts as an antagonist at the *N*-methyl-D-aspartate (NMDA) receptors, inhibits the reuptake of serotonin and noradrenaline, and promotes the blockade of nicotinic cholinergic receptors (28–30). These are additional mechanisms thought to play a role in methadone-mediated analgesia (30). Methadone has a duration of analgesic effect of approximately 4 h (31).

Tracheal intubation can stimulate coughing and gagging in patients, as well as a reflex sympathetic pressor response resulting in elevated HR and blood pressure (32). These reflexes may have adverse effects in patients with increased ICP. Intravenous lidocaine has been used in humans at doses of 1.5 to 2.5 mg/kg BW at least 3 min before induction with variable success to blunt the hemodynamic (pressor) and coughing responses to tracheal instrumentation (33,34). Although studies in dogs and cats failed to demonstrate similar effects, lidocaine was used for these reasons and for its potential neurological benefits (35,36). Lidocaine may reduce secondary brain injury by preventing sodium influx into ischemic neurons (37). Evidence suggests that infusion of antiarrhythmic doses (1.5 to 2 mg/kg BW, IV) after the onset of brain ischemia reduces neuronal death and improves neurologic outcome (38). Studies in dogs may have failed to demonstrate similar responses as those seen in humans, due to the lower dose (1 mg/kg BW, IV) administered (35). In addition to lidocaine, fentanyl and gabapentin have been reported to attenuate the sympathetic pressor response induced by laryngoscopy and tracheal intubation in humans (32,39).

During surgery the patient was placed in sternal recumbency for surgical site preparation with the head slightly elevated. Elevation of the head by 15° to 30° may improve cerebral venous drainage and limit cerebral venous congestion, thereby reducing ICP without decreasing CPP or CBF (40). Inversely, jugular vein occlusion may impair venous drainage causing increased ICP and was avoided except during jugular vein catheterization. Jugular occlusion was brief (< 15 s) and the patient's head and neck were kept straight throughout the procedure to prevent simultaneous occlusion of the contralateral jugular vein. Jugular catheterization of patients at risk of raised ICP is controversial; however, in this case the perioperative benefits of reliable vascular access were seen to outweigh the risks (40).

One important feature of a neuroanesthetic protocol is rapid anesthetic recovery to allow prompt neurological assessment (15). Anesthesia regimens including remifentanil allow earlier recovery and return of psychomotor function than those with fentanyl (41). The ultra-short half-life of remifentanil is advantageous for neurosurgical procedures as it allows for titration of the analgesic and anesthetic effects to varying noxious stimulation intensities (15,42). The side effects of remifentanil are dose-dependant and typical of the μ-opioid receptor agonist drugs (i.e., respiratory depression, decreased HR), but with a comparatively lower incidence of vomiting, which can increase ICP (43). Evidence from animal and human studies suggest that large doses of intraoperative remifentanil can promote hyperalgesia (44). These considerations, in addition to the high cost of remifentanil, favor transition to an alternative and longer-acting pain therapy following surgery, and as such, the patient was transitioned to methadone for postoperative pain (45).

Peak inspiratory pressure set between 10 to 12 cm H_2O, and RR was adjusted to maintain $PE'CO_2$ at 30 ± 2 mmHg. The $PaCO_2$ is an important factor in controlling cerebral vascular resistance (CVR) and CBF. An acute rise in $PaCO_2$ can cause a decrease in arteriolar pH resulting in decreased CVR which increases the CBF. In contrast, hypocapnia will result in intracranial vasoconstriction and decreased cerebral perfusion (40). Consequently ventilation strategies targeted a $PaCO_2$ between 34.1 and 36.4 mmHg (Table 1). Although IPPV may increase ICP by decreasing venous return from the head, maintaining PIP below 25 cm H_2O and positive-end-expiratory-pressure < 5 cm H_2O prevents clinically significant increases in ICP (46). The VDAlv/VT ranged from 14.6% to 24% (Table 1) and were not greater than the VDAlv/VT previously reported in unsedated tracheostomized dogs breathing quietly through an ETT (47).

Mean arterial pressure ranged from 80 to 110 mmHg. In the absence of direct ICP monitoring it is recommended that a MAP of 80 to 100 mmHg be maintained to ensure adequate CPP (14). Improved brain oxygenation in head trauma patients has been demonstrated when MAP is maintained above 90 mmHg, compared to patients managed similarly using 70 mmHg as the minimum acceptable MAP (48).

Intravenous 0.9% NaCl was administered at 5 to 10 mL/kg BW/h throughout anesthesia. Sodium chloride was selected over compound sodium lactate as the osmolality of 0.9% NaCl is closer to that of plasma and less likely to cause interstitial edema (14). Care should be taken to ensure electrolyte balances are maintained when administering 0.9% NaCl over a prolonged time period as electrolyte imbalances may occur. Except for the low pH observed at 315 min post-induction and 15 min post-extubation, electrolytes and blood-gas values were unremarkable. Hyperlactemia was present at each blood-gas evaluation and could be responsible for the low pH at 315 min post-induction and 15 min post-extubation. Although a peripheral venous lactate assay would have provided an adequate baseline measurement, unfortunately this was not evaluated to establish if the patient was hyperlactemic prior to anesthesia. The fact that this dog was receiving prednisolone could account for these findings as therapeutic doses of glucocorticoids can result in clinically relevant type-B hyperlactemia (49). To the authors' knowledge there are no incidences of type-B hyperlactemia associated with alfaxalone or remifentanil infusion reported in the literature. Hyperlactemia is reported in dogs with intracranial disease; in these cases, focal cerebral-ischemia and/or convulsions are potential type-A causes of lactic acidosis (50).

The failure to obtain a baseline preoperative pain score despite the fact that the patient was subjectively assessed as non-painful must be acknowledged. In addition, due to technical reasons, the first blood-gas evaluation did not occur until 45 min after induction of anesthesia. This delay prohibited accurate assessment of ventilation status prior to this time beyond that available from non-invasive parameters ($PE'CO_2$ and SpO_2).

In the present case, TIVA with alfaxalone and remifentanil was an acceptable alternative anesthetic technique to a propofol-based TIVA protocol for intracranial surgery. CVJ

References

1. Weglinski MR, Perkins WJ. Inhalational versus total intravenous anesthesia for neurosurgery: Theory guides, outcome decides. J Neurosurg Anesthesiol 1994;6:290–293.
2. Matta BF, Heath KJ, Tipping K, Summors AC. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. Anesthesiology 1999; 91:677–680.
3. Strebel S, Lam AM, Matta B, Mayberg TS, Aaslid R, Newell DW. Dynamic and static cerebral autoregulation during isoflurane, desflurane, and propofol anesthesia. Anesthesiology 1995;83:66–76.
4. Dershwitz M, Michalowski P, Chang Y, Rosow CE, Conlay LA. Postoperative nausea and vomiting after total intravenous anesthesia with propofol and remifentanil or alfentanil: How important is the opioid? J Clin Anesth 2002;14:275–278.
5. Bendtsen A, Kruse A, Madsen JB, et al. Use of a continuous infusion of althesin in neuroanaesthesia. Changes in cerebral blood flow, cerebral metabolism, the EEG and plasma alphaxalone concentration. Brit J Anaesth 1985;57:369–374.
6. Muir W, Lerche P, Wiese A, Nelson L, Pasloske K, Whittem T. Cardiorespiratory and anesthetic effects of clinical and supraclinical doses of alfaxalone in dogs. Vet Anaesth Analg 2008;35:451–462.
7. Baldy-Moulinier M, Besset-Lehmann J, Passouant P. Effects of combination alfaxalone and alfadolone, anesthetic derivatives of pregnanedione, on cerebral hemodynamics in cats. C R Seances Soc Biol Fil 1975;169:126–131.
8. Cohen RS, Nisbet HI, Creighton RE, Steward DJ, McDonald P. The effects of hypoxaemia on cerebral blood flow and cerebrospinal fluid pressure in dogs anaesthetized with Althesin, pentobarbitone and methoxyflurane. Can Anaesth Soc J 1973;20:757–762.
9. Glass PS, Gan TJ, Howell S. A review of the pharmacokinetics and pharmacodynamics of remifentanil. Anesth Analg 1999;89:S7–14.
10. Scott LJ, Perry CM. Remifentanil: A review of its use during the induction and maintenance of general anaesthesia. Drugs 2005;65: 1793–1823.
11. Musk GC, Flaherty DA. Target-controlled infusion of propofol combined with variable rate infusion of remifentanil for anaesthesia of a dog with patent ductus arteriosus. Vet Anaesth Analg 2007;34:359–364.
12. Bauquier SH, Culp WTN, Lin RC, Larenza MP. One-lung ventilation using a wire-guided endobronchial blocker for thoracoscopic pericardial fenestration in a dog. Can Vet J 2010;51:1135–1138.
13. Firth AM, Haldane SL. Development of a scale to evaluate postoperative pain in dogs. J Am Vet Med Assoc 1999;214:651–659.
14. Raisis AL, Leece EA, Platt SR, Adams VJ, Corletto F, Brearley J. Evaluation of an anaesthetic technique used in dogs undergoing craniectomy for tumour resection. Vet Anaesth Analg 2007;34:171–180.
15. Coles JP, Leary TS, Monteiro JN, et al. Propofol anesthesia for craniotomy: A double-blind comparison of remifentanil, alfentanil, and fentanyl. J Neurosurg Anesthesiol 2000;12:15–20.
16. Turner JM, Coroneos NJ, Gibson RM, Powell D, Ness MA, McDowall DG. The effect of althesin on intracranial pressure in man. Brit J Anaesth 1973;45:168–172.
17. Sari A, Maekawa T, Tohjo M, Okuda Y, Takeshita H. Effects of Althesin on cerebral blood flow and oxygen consumption in man. Brit J Anaesth 1976;48:545–550.
18. Bullock R, van Dellen JR, Campbell D, Osborn I, Reinach SG. Experience with Althesin in the management of persistently raised ICP following severe head injury. J Neurosurg 1986;64:414–419.
19. Ambros B, Duke-Novakovski T, Pasloske KS. Comparison of the anesthetic efficacy and cardiopulmonary effects of continuous rate infusions of alfaxalone-2-hydroxypropyl-β-cyclodextrin and propofol in dogs. Am J Vet Res 2008;69:1391–1398.
20. Ferre PJ, Pasloske K, Whittem T, Ranasinghe MG, Li Q, Lefebvre HP. Plasma pharmacokinetics of alfaxalone in dogs after an intravenous bolus of Alfaxan-CD RTU. Vet Anaesth Analg 2006;33:229–236.
21. Warne LN. Alfaxalone anesthesia in the cat. Proceedings of the 19th International Veterinary Emergency and Critical Care Symposium, San Diego, California, 2013:413–415.
22. Backonja M, Beydoun A, Edwards KR, et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: A randomized controlled trial. JAMA 1998;280:1831–1836.
23. Türe H, Sayin M, Karlikaya G, Bingol CA, Aykac B, Türe U. The analgesic effect of gabapentin as a prophylactic anticonvulsant drug on postcraniotomy pain: A prospective randomized study. Anesth Analg 2009;109:1625–1631.
24. Hay Kraus BL. Efficacy of maropitant in preventing vomiting in dogs premedicated with hydromorphone. Vet Anaesth Analg 2013;40:28–34.
25. de la Puente-Redondo VA, Siedek EM, Benchaoui HA, Tilt N, Rowan TG, Clemence RG. The anti-emetic efficacy of maropitant (Cerenia) in the treatment of ongoing emesis caused by a wide range of underlying clinical aetiologies in canine patients in Europe. J Small Anim Pract 2007;48:93–98.
26. Kristensen K, Christensen CB, Christrup LL. The mu1, mu2, delta, kappa opioid receptor binding profiles of methadone stereoisomers and morphine. Life Sci 1995;56:PL45–50.
27. Blancquaert JP, Lefebvre RA, Willems JL. Emetic and antiemetic effects of opioids in the dog. Eur J Pharmacol 1986;128:143–150.
28. Gorman AL, Elliott KJ, Inturrisi CE. The d- and l-isomers of methadone bind to the non-competitive site on the N-methyl-D-aspartate (NMDA) receptor in rat forebrain and spinal cord. Neurosci Lett 1997;223:5–8.
29. Codd EE, Shank RP, Schupsky JJ, Raffa RB. Serotonin and norepinephrine uptake inhibiting activity of centrally acting analgesics: Structural determinants and role in antinociception. J Pharmacol Exp Ther 1995;274:1263–1270.
30. Xiao Y, Smith RD, Caruso FS, Kellar KJ. Blockade of rat alpha3beta4 nicotinic receptor function by methadone, its metabolites, and structural analogs. J Pharmacol Exp Ther 2001;299:366–371.
31. Kerr C. Pain management I: Systemic analgesics. In: Seymour C, Duke-Novakovski T, eds. BSAVA Manual of Canine and Feline Anaesthesia and Analgesia. 2nd ed. Shurdington, Cheltenham, UK: British Small Animal Veterinary Association, 2007:89–103.
32. Gurulingappa, Aleem MA, Awati MN, Adarsh S. Attenuation of cardiovascular responses to direct laryngoscopy and intubation — A comparative study between IV bolus fentanyl, lignocaine and placebo (NS). J Clin Diagn Res 2012;6:1749–1752.
33. Tam S, Chung F, Campbell M. Intravenous lidocaine: Optimal time of injection before tracheal intubation. Anesth Analg 1987;66:1036–1038.
34. Sun L, Guo R, Sun L. The impact of prophylactic intravenous lidocaine on opioid-induced cough: A meta-analysis of randomized controlled trials. J Anesth 2014;28:325–333.
35. Jolliffe CT, Leece EA, Adams V, Marlin DJ. Effect of intravenous lidocaine on heart rate, systolic arterial blood pressure and cough responses to endotracheal intubation in propofol-anaesthetized dogs. Vet Anaesth Analg 2007;34:322–330.
36. Dyson DH. Efficacy of lidocaine hydrochloride for laryngeal desensitization: A clinical comparison of techniques in the cat. J Am Vet Med Assoc 1988;192:1286–1288.
37. Hemmings HC, Jr. Neuroprotection by Na^+ channel blockade. J Neurosurg Anesthesiol 2004;16:100–101.
38. Lei B, Popp S, Capuano-Waters C, Cottrell JE, Kass IS. Effects of delayed administration of low-dose lidocaine on transient focal cerebral ischemia in rats. Anesthesiology 2002;97:1534–1540.
39. Kaya FN, Yavascaoglu B, Baykara M, Altun GT, Gulhan N, Ata F. Effect of oral gabapentin on the intraocular pressure and haemodynamic responses induced by tracheal intubation. Acta Anaesthesiol Scand 2008;52:1076–1080.
40. Armitage-Chan EA, Wetmore LA, Chan DL. Anesthetic management of the head trauma patient. J Vet Emerg Crit Care 2007;17:5–14.
41. Takayama A, Yamaguchi S, Ishikawa K, et al. Recovery of psychomotor function after total intravenous anesthesia with remifentanil-propofol or fentanyl-propofol. J Anesth 2012;26:34–38.
42. Tipps LB, Coplin WM, Murry KR, Rhoney DH. Safety and feasibility of continuous infusion of remifentanil in the neurosurgical intensive care unit. Neurosurgery 2000;46:596–601; discussion 601–592.
43. Glass PSA, Hardman D, Kamiyama Y, et al. Preliminary pharmacokinetics and pharmacodynamics of an ultra-short-acting opioid: Remifentanil (GI87084B). Anesth Analg 1993;77:1031–1040.

44. Angst MS, Koppert W, Pahl I, Clark DJ, Schmelz M. Short-term infusion of the mu-opioid agonist remifentanil in humans causes hyperalgesia during withdrawal. Pain 2003;106:49–57.
45. Hachenberg T. Perioperative management with short-acting intravenous anesthetics. Anaesthesiol Reanim 2000;25:144–150.
46. Huynh T, Messer M, Sing RF, Miles W, Jacobs DG, Thomason MH. Positive end-expiratory pressure alters intracranial and cerebral perfusion pressure in severe traumatic brain injury. J Trauma 2002;53:488–492; discussion 492–483.
47. McDonell WN. Ventilation and acid-base equilibrium with methoxyflurane anesthesia in dogs [MSc dissertation]. Guelph, Canada, University of Guelph, 1969.
48. Narayan RK, Michel ME, Ansell B, et al. Clinical trials in head injury. J Neurotrauma 2002;19:503–557.
49. Boysen SR, Bozzetti M, Rose L, Dunn M, Pang DS. Effects of prednisone on blood lactate concentrations in healthy dogs. J Vet Intern Med 2009;23:1123–1125.
50. Sullivan LA, Campbell VL, Klopp LS, Rao S. Blood lactate concentrations in anesthetized dogs with intracranial disease. J Vet Intern Med 2009;23:488–492.

Answers to Quiz Corner
Les réponses du test éclair

1. **d)** Answers "a" and "c" are differential diagnoses for miliary dermatitis but not the most common cause, answer "b" is not common at all in the cat, and answer "e" does not present as miliary dermatitis.

d) Les réponses "a" et "c" représentent des diagnostics différentiels pour la dermatite miliaire, mais non la cause la plus commune; la réponse "b" n'est vraiment pas la plus commune chez le chat et la réponse "e" ne se présente pas comme une dermatite miliaire.

2. **d)** The choice of inhalation agent will not affect the accuracy of the pulse oximeter. Bright room lights, movement, and vasoconstriction (no blood flow under the probe) will affect the accuracy.

d) Le choix de l'agent d'inhalation n'affecte pas l'exactitude de l'oxymètre de pouls. Les lumières vives de la salle, le mouvement et la vasoconstriction (pas le débit sanguin sous la sonde) vont affecter l'exactitude.

3. **a)** All the conditions in answer "a" tend to be associated with an elevated ionized calcium concentration. An ionized calcium concentration is usually normal in hyperadrenocorticism, low in hypoparathyroidism, and normal to low in hypovitaminosis D.

a) Tous les problèmes énumérés à la réponse "a" ont tendance à être associés à une concentration de calcium ionisé élevée. Une concentration de calcium ionisé est habituellement normale lors d'hyperadrénocorticisme, basse lors d'hypoparathyroïdisme et normale à basse lors d'hypovitaminose D.

4. **b)** Clean-contaminated operations involve a controlled entry into the gastrointestinal (GI), respiratory, or genitourinary tracts. There were no complications associated with this operation, indicating that there was no gross spillage of bronchial contents into the surgical field. If that had occurred, this operation would have been considered contaminated. Clean operations are those that do not involve the GI, respiratory, or genitourinary tracts. Dirty operations involve traumatic manipulations with necrotic and infected tissues. Infection may occur over time, but is used to classify a surgical procedure.

b) Des chirurgies propres-contaminées impliquent une entrée contrôlée dans les systèmes gastro-intestinal, respiratoire ou génito-urinaire. Il n'y avait pas de complications associées à cette chirurgie indiquant qu'il n'y avait pas de déversement de contenu bronchique dans le champ opératoire. Si cela c'était produit, cette chirurgie aurait été considérée contaminée. Les chirurgies propres sont celles qui n'impliquent pas les systèmes gastro-intestinal, respiratoire ou génito-urinaire. Les chirurgies souillées impliquent des manipulations traumatiques aux tissus nécrotiques et infectés. Une infection peut se produire de temps en temps, mais elle est utilisée pour classifier une procédure chirurgicale.

5. **d)** SCC is the most common tumor of the equine external genitalia and is rarely found in the other listed locations.

d) Le carcinome spino-cellulaire est la tumeur la plus commune des organes génitaux du cheval et est rarement observé dans les autres endroits énumérés.